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 Ser Asn Phe Gly Trp Glu Thr Lys Ile Lys Ala Trp Met Asp Arg Tyr

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Met Lys Arg Ser Gly Arg Met Asn Tyr Met Cvs Pro Asn Ser Ser Met Asn Tyr Met Cvs Pro Asn Ser Ser Met	'h w
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Tyr																
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Pro I	u	ac u	שבו	12	205	eu s	er 1	rhr (Glu /	Asn (Gly (Glu G	Slu (Glu	Glu	Glu
Gln S																
Thr C																
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Ala A	la T	hr	Thr	Se	r L	eu A:	ra A	ra A	la A	en C	275	1	•			1280
Slu T	yr S	er	Lys	Ly	s A	la A	la M	et L	ys P	ro L	ys P	ro L	eu S	er t	.235 7al T	ev
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Ala Pro Ser Leu Asp Asp Pro Ala Arg Arg His Met Thr Ile His Val

Pro Leu Asp Ala Ser Arg Ser Lys Gln Leu Ile Ser Glu Trp Lys Gln 70 75

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Ala Ser Ser Ser Leu Leu Asn Arg Leu Gln Leu Asp Asp Asp Ile

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38	5						390													
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		-						ב ע כ												Gly
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Leu		_							<b>5</b> × 11	Pr	0 :							<b>S</b>		
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Ala					Leu															
Leu			he :	Leu	, 2 3						- 7	חגי								
Asp		I.	le :																	
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Gly : 785								/ >						~ ~ .						
						/ <b>7</b> U	,						705							
Gln 1	Phe	Pı	0 I	Leu	Gly 805	Phe	Vā	al A	Ala	Arg	r Va	al .	Phe	As	sp M	let	Ile		ne I	en 100
3ln (	31y	Th	ır G	lu	Val	Ile	Ph	ıe I	.ys	Val	8.	10 פו	Ι.Α	e.	. ~ T		T	81	15	

825 830 His Lys Pro Leu Ile Leu Gln His Glu Asn Leu Glu Thr Ile Val Asp 845 840 Phe Ile Lys Ser Thr Leu Pro Asn Leu Gly Leu Val Gln Met Glu Lys Thr Ile Asn Gln Val Phe Glu Met Asp Ile Ala Lys Gln Leu Gln Ala 875 870 Tyr Glu Val Glu Tyr His Val Leu Gln Glu Glu Leu Ile Asp Ser Ser 885 890 Pro Leu Ser Asp Asn Gln Arg Met Asp Lys Leu Glu Lys Thr Asn Ser 900 905 Ser Leu Arg Lys Gln Asn Leu Asp Leu Leu Glu Gln Leu Gln Val Ala 920 Asn Gly Arg Ile Gln Ser Leu Glu Ala Thr Ile Glu Lys Leu Leu Ser 930 935 940 Ser Glu Ser Lys Leu Lys Gln Ala Met Leu Thr Leu Glu Leu Glu Arg 950 955 Ser Pro Ala Ala Asp Gly Gly Gly Ala Ala Ala Glu Arg Arg Ala 970 Gln Arg Pro Gly Ala 980 <210> 5919 <211> 1320 <212> DNA <213> Homo sapiens <400> 5919 ggctgctgca tcttctccgc gctatggctg cgttcggccg tcaggaaatt aaagagggtg ctttactgtt gccctgaaat tttcaccatg cgccagcagg acattaacga cactgtcagg cttctcaagg agaagtgcct tttcacggta cagcaagtca ccaagatttt gcacagttgc ccctctgttc ttcgagagga cctgggtcaa ctggaataca agtttcagca gcctcgtctt acagcgtgac tgcaaagaaa aagacttttg ttttgcaaaa gaaaagcagc tcggtgactc cgtccacatc gccacagttg agtcagatgg cagtggcagt cctttgccag tggaaggagt tectgetaag gggaggtgea ggaggaetaa tttattattg tgeaactgee agteetgege attccagcta cgctaagcgc cctgcccagg cacgtaacaa aacatagacc tgttttgaag tggcttgtta cccaagggtg cctcactcat ctgcgccacc aggaagatga actgtgaggg ctcctataag gggcaggaag agcaaagctg tcctaggcca accagagatt catctttcat gcagtgacat gttgataaaa aatgatggtc agtatgaaac tggtaacagg ttgtagatgg ctttctatgg tatatcccag tctcttgcaa acgattgtga agaatgccag tgttgtttaa gattcggcag tttgtgtggg gaggtggggg caggatgggg tttggttgcc aaaagagttt 780

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340 345	rys rys IIe
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Th	r GI	y As	n Il	е Ту	r Ty	r Al	a Ar	g Se	r Gl	y Th	r Ly	s Il	e Il	e Gl	/ Lys
			TO	U				7.0	5					_	
		11	.uy .5	S FII	E 111.	г те	u 11.	e As∶ ∩	p GI	y II	e Ar			a Thi	Gly
Se	r Ty			e Th	r Tri	o Th	r Ası	o മദി	v t.v	s I.o.	11 Act	12!	5 • 0		1 Leu
		U				13	5				1//	`			
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Sei	Lys	Gl			Leu	Glv	/ Asr	1 J.e.	) 1 T.A.	1 720	· Mat		190		Arg
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		,				215	•				220				
225	r GTŽ	/ цу	s Ala	Glu	Arg	Lys	Pro	His	Asp	Cys	Glu	Ser	Ser	Thr	Val
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		. 01.	ı Asp	245	PILE	ser	ser	HIS	250	Asp	Glu	Leu	Gln		Arg
Lys	Ala	Ile	Asp	Ala	Ala	Thr	Gln	Thr	250 Glu	Pro	Glv	C1	~1	255	_
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Ile	Arq		Thr	Asp	Phe	Hic	360	Dwa	<b>~</b> 1	·	_	365			
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Gly Tyr Gly Ser Cys Arg Asp Thr Gln Ser Trp Thr Pro Asp Pro Leu
Pro His Pro Pro Ser Leu Ser Pro Gln Ser Leu Leu Tyr Ser Gln Ala
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Lys Leu Arg Phe Glu Asp Thr Leu Glu Phe Val Gly Phe Asp Ala Lys
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1320

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Gly Glu Arg Pro His 545	Lys Cys Asn 550	Glu Cys Gly 555	Lys Ser	Phe Ile	Gln 560
Ser Ala His Leu Ile 565	Gln His Gln	Arg Ile His 570	Thr Gly	Glu Lys 575	Pro
Phe Arg Cys Glu Glu 580	Cys Gly Lys	Ser Tyr Asn 585	Gln Arg	Val His 590	Leu
Thr Gln His Gln Arg 595	600		605	_	
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Ser Val His Ser Gly 625	Glu Arg Pro 630	Phe Lys Cys 635	Asn Glu	Cys Gly	Lys 640
Gly Phe Gly Arg Arg 645	Ser His Leu	Ala Gly His 650	Leu Arg	Leu His 655	Ser
Arg Glu Lys Ser His 660	Gln Cys Arg	Glu Cys Gly 665	Glu Ile	Phe Phe 670	Gln
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Ile Cys Gly Lys Ala 725	-	Ser Ser Asp 730	Leu Ile	Gln His 735	Tyr
Arg Thr His Thr Ala 740	Glu Lys Pro	Tyr Gln Cys 745	Asp Ile	Cys Arg 750	Glu
Asn Val Gly Gln Cys 755	760	•	765		
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Glu .			241	,					- 7	145										
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								361	)						200					
							3/5							200						
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Asn F	he i	Met	His	Ası	a L	eu	Leu	Pro	M	et	Gln	As	sn 1	Leu	Gln	Pr	ים	'h~	ر دی	3.7
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5289

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90

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Glu Ile Leu His His Leu Ser Glu Arg Asn Arg Val Arg Asp Arg Asp
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Val Tyr Leu Val Ile Glu Asp Leu Lys Gln Lys Ala Ser Glu Tyr Glu
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Val Asp Ser Ala Val Ala Leu Glu Thr Lys Asp Thr Ser Leu Ala Ser
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Phe Ile Pro Ala Val Asn Asp Leu Thr Ser Asp Leu Phe Arg Thr Lys
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Ser Lys Ser Glu Glu Ile Lys Ile Glu Leu Glu Lys Leu Glu Lys Asn
Leu Thr Ala Thr Leu Val Leu Glu Lys Cys Leu Gln Glu Asp Val Lys
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                                   170
Lys Ala Glu Leu His Leu Ser Thr Glu Arg Ala Lys Val Asp Asn Arg
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Arg Gln Asn Met Asp Phe Leu Lys Ala Lys Ser Glu Glu Phe Arg Phe
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Gly Ile Lys Ala Ala Glu Glu Gln Leu Ser Ala Arg Gly Met Asp Ala
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Ser Leu Ser His Gln Ser Leu Val Ala Leu Ser Glu Lys Leu Ala Arg
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Leu Lys Gln Gln Thr Ile Pro Leu Lys Lys Lys Leu Glu Ser Tyr Leu
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Arg Pro Leu Leu Lys Asp Ala Ala His Pro Ser Glu Ala Thr Phe Ser
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Cys Asp Cys Val Ala Asp Ala Leu Ile Leu Arg Val Arg Ser Glu Leu
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120

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115

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ccagtccaga 2220	gccctcaagc	tettgtggee	atggagaagg	aggaaaaaga	gagtcccttc

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145					150					155					160
Ala	Trp	Met	Val	Lys	Arg	Trp	Ala	Glu	Gly	Ala	Glu	Ser	Leu	Glu	Val
				165					170					175	
Leu	Ala	Glu	Arq	Glu	Ser	Leu	Tyr	Gln	Leu	Leu	Ser	Gln	Thr	Ser	Pro
			180				•	185					190		
C1.,	7.00	Mot		λνα	Λcn	Val	77.5		ጥኒያ	Glv	T.611	Acn		Ala	Thr
GIU	ASII		піз	Arg	ASII	vai		GIII	TYL	Gry	Leu		FIU	AIG	1111
		195				_	200				_	205			_
Arg	Tyr	Pro	Asn	Leu	Asn	Leu	Arg	Ala	Val	Thr	Pro	Asn	GIn	Val	Arg
	210					215					220				
Asp	Leu	Tyr	Asp	Val	Leu	Ala	Lys	Glu	Pro	Val	Gln	Arg	Asn	Asn	Asp
225					230					235					240
Lvs	Thr	Asp	Thr	Glv	Met	Pro	Ala	Thr	Glv	Ser	Ala	Glv	Thr	Gln	Glu
-2-				245					250			•		255	
C1.,	7.011	T OU	7 ~~		Cvc	Gla	G1.,	Gla		λla	Glaz	ጥኒኒዮ	Pro	Gly	Va I
GIU	Deu	пец	_	пр	Cys	GIII	Giu		* * * * *	AIG	Cry	- Y -	270	Ory	Val
		_	260	_	_	_	_	265		_	~ 3				_
His	Val	Ser	Asp	Leu	Ser	Ser		Trp	Ala	Asp	GIA		Ala	Leu	Cys
		275					280					285			
Ala	Leu	Val	Tyr	Arg	Leu	Gln	Pro	Gly	Leu	Leu	Glu	Pro	Ser	Glu	Leu
	290					295					300				
Gln	Gly	Leu	Gly	Ala	Leu	Glu	Ala	Thr	Ala	Trp	Ala	Leu	Lys	Val	Ala
305	-		-		310					315			_		320
	Δen	Glu	T.e.11	Glv		Thr	Pro	Va 1	Val		Δla	Gln	Δla	Val	
GIU			عاد تا	325				• • • •	330			<b></b>	•••	335	
	<b>63</b>		3		T	~1	*	<b>*1</b> ~			* ~	C	TT-1 -		TT: -
Ala	GIY	ser	_	Pro	Leu	GIY	Leu		Ala	Tyr	ьеи	ser		Phe	HIS
	_		340					345					350		
Ser	Ala	Phe	Lys	Ser	Met	Ala	His	Ser	Pro	Gly	Pro	Val	Ser	Gln	Ala
		35 <b>5</b>					360					365			
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	370					375					380				
Thr		Gln	Arq	Ser	Arq		Lys	Asp	Leu	Leu		Glu	Asn	Ala	Glu
		Gln	Arg	Ser			Lys	Asp	Leu			Glu	Asn	Ala	
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Ser Pro Gly Phe 465 Pro Gln	Leu Ala Thr Ser Glu 450 His Gly His	Gly Glu Gln 435 His Arg Gly Leu	Gly Val 420 His Leu Ser Tyr Pro 500	Lys 405 Pro Gln Tyr Cys Glu 485 Gln	390 Lys Pro Glu Val Phe 470 Gln Thr	Ala Leu Asp Ala Leu 455 Arg His	Arg Pro Gly 440 Glu Cys Pro	Leu Glu 425 Ala Arg His Gly Lys 505	Glu 410 Pro Gly Leu Thr Asp 490 Ala	395 Met Gly Asp Cys 475 Gly Glu	Glu Val Leu Val 460 Glu His	Ala Pro Cys 445 Asn Ala Phe Ser	Glu Leu 430 Ala Gly Thr Tyr Asp 510	Thr 415 Thr Leu His Leu Cys 495 Arg	400 Pro Pro Cys Phe Trp 480 Leu
Ser Pro Gly Phe 465 Pro Gln	Leu Ala Thr Ser Glu 450 His Gly His	Gly Glu Gln 435 His Arg Gly Leu	Gly Val 420 His Leu Ser Tyr Pro 500	Lys 405 Pro Gln Tyr Cys Glu 485 Gln	390 Lys Pro Glu Val Phe 470 Gln Thr	Ala Leu Asp Ala Leu 455 Arg His	Arg Pro Gly 440 Glu Cys Pro	Leu Glu 425 Ala Arg His Gly Lys 505	Glu 410 Pro Gly Leu Thr Asp 490 Ala	395 Met Gly Asp Cys 475 Gly Glu	Glu Val Leu Val 460 Glu His	Ala Pro Cys 445 Asn Ala Phe Ser Ser	Glu Leu 430 Ala Gly Thr Tyr Asp 510	Thr 415 Thr Leu His Leu Cys 495 Arg	400 Pro Pro Cys Phe Trp 480 Leu
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Ser Pro Gly Phe 465 Pro Gln Pro Gly Asp 545	Leu Ala Thr Ser Glu 450 His Gly His Glu Leu 530 Pro	Gly Glu Gln 435 His Arg Gly Leu Ser 515 Ser	Gly Val 420 His Leu Ser Tyr Pro 500 Pro Thr	Lys 405 Pro Gln Tyr Cys Glu 485 Gln Glu Pro	390 Lys Pro Glu Val Phe 470 Gln Thr Leu Thr	Ala Leu Asp Ala Leu 455 Arg His Asp Pro Ala 535 Arg	Arg Pro Gly 440 Glu Cys Pro His Thr 520 Ser	Leu Glu 425 Ala Arg His Gly Lys 505 Pro Gln Gln	Glu 410 Pro Gly Leu Thr Asp 490 Ala Ser Glu Ile	395 Met Gly Asp Cys 475 Gly Glu Glu Gly Arg 555	Gln Glu Val Leu Val 460 Glu His Gly Asn Ala 540 Leu	Ala Pro Cys 445 Asn Ala Phe Ser Ser 525 Gly Ser	Glu Leu 430 Ala Gly Thr Tyr Asp 510 Met Pro Ser	Thr 415 Thr Leu His Leu Cys 495 Arg Pro Val	400 Pro Pro Cys Phe Trp 480 Leu Gly Pro Pro Glu 560
Ser Pro Gly Phe 465 Pro Gln Pro Gly Asp 545	Leu Ala Thr Ser Glu 450 His Gly His Glu Leu 530 Pro	Gly Glu Gln 435 His Arg Gly Leu Ser 515 Ser	Gly Val 420 His Leu Ser Tyr Pro 500 Pro Thr	Lys 405 Pro Gln Tyr Cys Glu 485 Gln Glu Pro Pro	390 Lys Pro Glu Val Phe 470 Gln Thr Leu Thr	Ala Leu Asp Ala Leu 455 Arg His Asp Pro Ala 535 Arg	Arg Pro Gly 440 Glu Cys Pro His Thr 520 Ser	Leu Glu 425 Ala Arg His Gly Lys 505 Pro Gln Gln	Glu 410 Pro Gly Leu Thr Asp 490 Ala Ser Glu Ile Thr	395 Met Gly Asp Cys 475 Gly Glu Glu Gly Arg 555	Gln Glu Val Leu Val 460 Glu His Gly Asn Ala 540 Leu	Ala Pro Cys 445 Asn Ala Phe Ser Ser 525 Gly Ser	Glu Leu 430 Ala Gly Thr Tyr Asp 510 Met Pro Ser	Thr 415 Thr Leu His Leu Cys 495 Arg Pro Val Pro	400 Pro Pro Cys Phe Trp 480 Leu Gly Pro Pro Glu
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C - w	~1	7. ~~~	Dwa	165	T	17-1	7 an	. ה		Cl n	ח ה	7 ~~	C1 5		Luc
Ser	GIU	Arg		IIII	Lys	Val	ASII	185	Ser	GIII	AIA	Arg	190	FIIC	цуз
Due	C	т1.	180	~7	т1.	3	Dho		The	700	T 011	Tlo		T 011	C111
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3703	2	195	C	7 0	T 0	~1	200	T1~	Th~	C1	T 011		212	Val	17 n 1
vai		ser	ser	Leu	Leu		Tyr	ıyı	Inr	GIU	220	Asp	Ald	vaı	vai
•	210	<b>~1</b>	**- 7	T	7	215	7	37-3		C		T	The	C ~ ~	T 011
	HIS	GIY	vai	Lys	Asp	ьys	Pro	vai	Leu		Leu	Lys	Inr	ser	
225	3			<b>.</b>	230	~1	3	N	77-	235	77-	~1	T	7	240
TIE	Asp	мет	Asn	-	Ile	GIU	Asp	Asp		ıyı	Ald	Gru	Lys		GLY
<b></b>	<b>~</b> 3			245	<b>.</b>	<b>3</b>	*	<b>T</b>	250		C	21.	17-7	255	C1
Cys	GIY	Met		ser	Leu	ASI	гÀг		Pne	ser	ser	AIA		Leu	GIA
<b>~</b> 1	<b>a</b> 3	D	260	3	<b>~1</b>	<b></b>	Dh.a	265	T	7	D		270	T	<b>T</b> 1.
GIU	GIA		Asn	Asn	Gly	Tyr		Asp	ьуs	Leu	Pro		GIU	Leu	iie
<b>-</b> 1 -	<b>.</b>	275		•	•••	•	280	•	<b>5</b>		<b>*</b>	285	3	<b>7</b>	21-
GIN		TTE	Leu	Asn	His		Thr	Leu	Pro	Asp		Cys	Arg	Leu	Ala
<b>~</b> 1	290	<b>a</b>	•	•	•	295	<b>~1</b>	•••	<b>G</b>	<b>G</b>	300	D	T	<b>01</b>	<b></b>
	Thr	Cys	Lys	Leu	Leu	Ser	GIn	HIS	cys		Asp	Pro	Leu	GIN	
305					310			-		315	•		•	m\	320
ire	His	Leu	Asn		Gln	Pro	Tyr	Trp		гÀг	Leu	Asp	Asp		Ser
_	~1	51	_	325	<b>.</b>	•	<b>~</b>	<b></b>	330		~1	<b></b>	•	335	<b>.</b>
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_	_	1	340	_	_	-1	-,	345	_	••• •		~1	350	<b>5</b>	•
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Pro	Asn	Leu	GIn		Leu	Asn	Leu	ser		Cys	Asp	ьуs	Leu		Pro
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GIN	AIA	Pne		HIS	Ile	ALA	rys		Cys	ser	Leu	гЛS		Leu	vai
<b>-</b>		•	420	•	**- *	<b>~</b> 1	<b>~1</b>	425		•		<b>a</b>	430	•	<b>.</b>
Leu	Tyr	_	Inr	гÀг	Val	GIU		Inr	Ala	Leu	Leu		iie	Leu	ASI
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Pne	_	Ser	GIU	Leu	Gln		Leu	ser	Leu	GIY		Cys	vaı	Met	ire
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Leu	Arg	1111	Leu		Leu	пр	Arg	Cys		ASII	116	1111	Gru		GIY
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A:	rg	Pr	0 1	\la	G1	lu T	yr	Asp	Pr	o L	vs	<b>Δ</b> 1:	⊥ a. T.∉	70	Mat	- 7.7		- 7 .			175	His
Se	er	Ηi	s A	lrg	Il	e A	rg	Phe	Ly	s L	eu	Lys	- 5 A:	ca	Pro	) I.e	-11 G	:711	19	יט הר	11.,	Gly
Ai	g	AS	ps o	er	Ly	s A	la :	Leu	۷a	1 G	lu	Let	ı As	sn ·	Gly	' Va	ıls	er	Le	u I	le	Pro
22	:5	<b>υ</b> Ξ.	, ,	e.r	MI	y As	sp (	230	G1;	y Le	eu	His	G1	У (	Gln	Al	a P	ro	Ly	s V	al	Pro
						24	. O .		111.	LAI	a	Inr	Se	r	Ser	Se	r M	et	Al.	a S	er	240 Phe
Le	u	Туз	: s	er	Th			eu	Pro	o As	n	Hie	25 זג	· ·	T 1 _	7	_ ~		_	2	55	Gln
Gl	u .	Ala	P:	ro	Se	r Cy	's I	ro	Let	ı Al	a	Pro	Se	r A	asA	Le	n G	1 37	27	, .	~ ~	Arg
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Lys	3	rp	As	q	Ala	Ph	e I	le	Lvs	Gli	, ,	Γhγ-	330	, ₇	~	<b>-</b> 7-	_			33	35	
Glı	1 (	Cys	Va	1	Gln	Il	e L	eu	Phe	Ası	n 5	Ser	Arc	т	vr	Δ1=	. G1		350	· .		~ 1
ret	16	Hy	As	n i	Met	Va:	l P	ro '	Val	Pro	<b>T</b>	yr	Arg	L	ys	Ile	Al	a (	Cvs	Δς	n i	Pro
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						Gl ₃																
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Thr	G	ly	Ası	n I	Ys	Phe	Th	r I	ys	Asp	T	hr '	Thr	Lv	/S	Γ. <del>.</del>	Gli	. D	30	ות	_ ^	
Pro	P:	ro 50	GΙι	ב	Asp	Thr	Se	r A	la	Glu	V	al s	Ser	Ar	gi	Ala	Thi	· v	al	Lei	ιA	sn
Leu 465			G+ )	, A	SII	Ата	47	g s	er	Asp	L	ys (	Зlу	Se	rı	1et	Sex	G	lu	Ası	, C	ys
Gly																						
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Pro	Th	ır :	Ser	G	lu -	Glu	Me	t T	hr i	Asp	Se	r M	let	Pr	0 6	10	ui a	5. T.	10	D 5	_	
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Glu 545	AS	ρį	чта	A	rg :	Pro	Gli	1 G	lu A	Arg	Pr	o V	al	Glı	ı A	sp	Ser	Ні	is	Glv	As	g d
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le	As	p	Phe	L 5	eu 00	Gln	Ala	Lys	s M	et	Asp	G]	ln 1	Pro	Al	a I	ys	Lys	4 L	95 ys	Lys
al.	Pr	0	Leu			Tyr	Asn	Gli	ı L	eu	505 Lys	Le	eu A	Ala	Le	u G	lu	510 Lys	G	lu	Lys
la	Ar	g				Glu				20							2 -				
eu .		_				Arg			•						- 4	^					
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la :	Ile	<i>!</i>	/al	Αı	gs	Ser	Pro	Glu	H	is (	31 n	D۳						C	. د	, <b>.</b>	

			580					585					590		
Ala	Pro	Pro 595	Ser	Ser	Arg	Arg	Lys 600	Glu	Ser	Ser	Thr	Pro 605	Glu	Glu	Phe
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	690			_	Leu	695		_			700				
705		_	_		Lys 710					715	_		_		720
_	_	_		725	Tyr				730	_		_		735	
•	-		740		Arg			745		_			750		
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Ala	Ser 770	Glu	Leu	Ala	Asn	Thr 775	Ala	Lys	Ala	Asp	Val 780	Pro	Tyr	Ile	Leu
785					Pro 790				_	795		_	_		800
•				805	Ser				810					815	
			820		Ala			825			_		830		
	_	835	_		Leu		840				_	845			_
_	850				Asn	855					860	_			
865					Glu 870					875					880
				885	Pro	_		_	890					895	
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	_	915		_	Val	-	920		-			925			
	930				Pro	935					940				
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			980		Cys			985					990		
Cys	Ser	Cys 995	Ile	His	Phe	Thr	Asn 1000		Ser	Ile	Leu	Ile 100		Thr	Asn
Lys	Phe	Tyr	Glu	Ile	Asp	Met	Lys	Gln	Tyr	Thr	Leu	Glu	Glu	Phe	Leu

1010 1015 Asp Lys Asn Asp His Ser Leu Ala Pro Ala Val Phe Ala Ala Ser Ser 1030 1035 Asn Ser Phe Pro Val Ser Ile Val Gln Val Asn Ser Ala Gly Gln Arg 1045 1050 Glu Glu Tyr Leu Leu Cys Phe His Glu Phe Gly Val Phe Val Asp Ser 1060 1065 Tyr Gly Arg Arg Ser Arg Thr Asp Asp Leu Lys Trp Ser Arg Leu Pro 1075 1080 Leu Ala Phe Ala Tyr Arg Glu Pro Tyr Leu Phe Val Thr His Phe Asn 1095 1100 Ser Leu Glu Val Ile Glu Ile Gln Ala Arg Ser Ser Ala Gly Thr Pro 1105 1110 1115 Ala Arg Ala Tyr Leu Asp Ile Pro Asn Pro Arg Tyr Leu Gly Pro Ala 1125 1130 1135 Ile Ser Ser Gly Ala Ile Tyr Leu Ala Ser Ser Tyr Gln Asp Lys Leu 1140 1145 Arg Val Ile Cys Cys Lys Gly Asn Leu Val Lys Glu Ser Gly Thr Glu 1155 1160 1165 His His Arg Gly Pro Ser Thr Ser Arg Ser Ser Pro Asn Lys Arg Gly 1175 1180 Pro Pro Thr Tyr Asn Glu His Ile Thr Lys Arg Val Ala Ser Ser Pro 1185 1190 1195 Ala Pro Pro Glu Gly Pro Ser His Pro Arg Glu Pro Ser Thr Pro His 1205 1210 Arg Tyr Arg Glu Gly Arg Thr Glu Leu Arg Arg Asp Lys Ser Pro Gly 1220 1225 1230 Arg Pro Leu Glu Arg Glu Lys Ser Pro Gly Arg Met Leu Ser Thr Arg 1240 Arg Glu Arg Ser Pro Gly Arg Leu Phe Glu Asp Ser Ser Arg Gly Arg 1255 1260 Leu Pro Ala Gly Ala Val Arg Thr Pro Leu Ser Gln Val Asn Lys Val 1270 1275 Trp Asp Gln Ser Ser Val 1285 <210> 6247 <211> 497 <212> DNA <213> Homo sapiens <400> 6247 geggeegeag egetgaatgg ggtggaeega egtteeetge agegtteaca aggetggete tagaagtgct ggagagggcc aagaggaggg cggtggactg gcatgccctg gagcgtccca aaggetgeat gggggteett geeegggagg egeeeeacet agagaaacag eeggeageeg gcccgcagcg cgttctcccg ggagagaaat attattcatc tgtgccagag gaaggagggg caacccatgt ctatcgttat cacagaggcg agtcgaagct gcacatgtgc ttggacatag ggaatggtca gagaaaagac agaaaaaaga catcccttgg tcctggaggc agctatcaaa

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205

195

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His Ala Asn Glu Arg Met Leu Phe His Gly Ser Pro Phe Val Asn Ala
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Ala Leu Ala Glu Tyr Val Ile Tyr Arg Gly Glu Gln Ala Tyr Pro Glu
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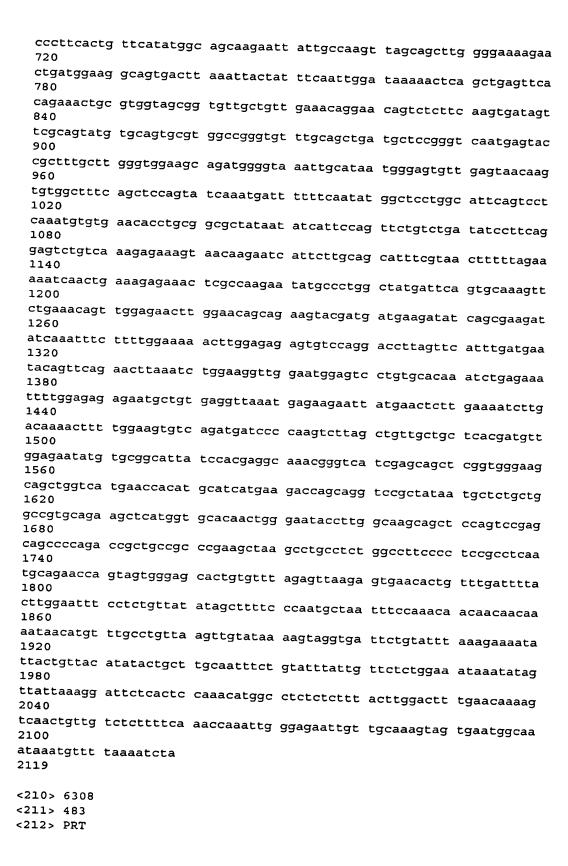
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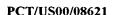
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#### What is claimed is:

- 1. An isolated nucleic acid molecule encoding a polypeptide comprising an aminacid sequence that is at least 85% identical to a polypeptide including an amino acid sequence selected from the group consisting of SEQ ID NO:2n, wherein n is any integer 1-3161, or the complement thereof.
- 2. The isolated nucleic acid molecule of claim 1, said molecule hybridizing under stringent conditions to a nucleic acid sequence complementary to a nucleic acid molecule comprising the sequence of nucleotides selected from the group consisting of SEQ ID NO:2n-wherein n is any integer 1-3161, or the complement thereof.
- 3. The isolated nucleic acid molecule of claim 1, said molecule encoding a polypeptide comprising the amino acid sequence selected from the group consisting of SEQ II NO: 2n, wherein n is any integer 1-3161, or an amino acid sequence comprising one or more conservative substitutions in the amino acid sequence selected from the group consisting of SI ID NO: 2n.
- 4. The isolated nucleic acid molecule of claim 1, wherein said molecule encodes a polypeptide comprising the amino acid sequence selected from the group consisting of SEQ II NO: 2n, wherein n is any integer 1-3161.
- 5. The isolated nucleic acid molecule of claim 1, wherein said molecule comprise the sequence of nucleotides selected from the group consisting of SEQ ID NO:2*n*-1, wherein *i* any integer 1-3161, or the complement thereof.
- 6. An oligonucleotide less than 100 nucleotides in length and comprising at least contiguous nucleotides selected from the group consisting of SEQ ID NO:2n-1, wherein n is a integer 1-3161, or the complement thereof.
  - 7. A vector comprising the nucleic acid molecule of claim 1.

- 8. The vector of claim 7, wherein said vector is an expression vector.
- A host cell comprising the isolated nucleic acid molecule of claim 1.
- 10. A substantially purified polypeptide comprising an amino acid sequence at least 80% identical to a polypeptide comprising the amino acid sequence selected from the group consisting of SEQ ID NO: 2n, wherein n is any integer 1-3161.
- 11. The polypeptide of claim 10, wherein said polypeptide comprises the amino acid sequence selected from the group consisting of SEQ ID NO: 2n, wherein n is any integer 1-3161.
  - 12. An antibody that selectively binds to the polypeptide of claim 10.
- 13. A pharmaceutical composition comprising a therapeutically or prophylactically effective amount of a therapeutic selected from the group consisting of:
  - a) the nucleic acid of claim 1;
  - b) the polypeptide of claim 10; and
  - c) the antibody of claim 12;
  - and a pharmaceutically acceptable carrier.
- 14. A kit comprising in one or more containers, a therapeutically or prophylactically effective amount of the pharmaceutical composition of claim 13.
- 15. A method of producing the polypeptide of claim 10, said method comprising culturing the host cell of claim 9 under conditions in which the nucleic acid molecule is expressed.
- 16. A method of detecting the presence of the polypeptide of claim 10 in a sample, comprising contacting the sample with a compound that selectively binds to said polypeptide under conditions allowing the formation of a complex between said polypeptide and said



compound, and detecting said complex, if present, thereby identifying said polypeptide in said sample.

- 17. A method of detecting the presence of a nucleic acid molecule of claim 1 in a sample, the method comprising contacting the sample with a nucleic acid probe or primer that selectively binds to the nucleic acid molecule and determining whether the nucleic acid probe of primer bound to the nucleic acid molecule of claim 1 is present in the sample.
- 18. A method for modulating the activity of the polypeptide of claim 10, the method comprising contacting a cell sample comprising the polypeptide of claim 10 with a compound that binds to said polypeptide in an amount sufficient to modulate the activity of the polypeptid
- 19. The use of a therapeutic in the manufacture of a medicament for treating a syndrome associated with a ORFX-associated disorder, wherein said therapeutic is selected fro the group consisting of:
  - a) the nucleic acid of claim 1;
  - b) the polypeptide of claim 10; and
  - c) the antibody of claim 12.
- 20. A method for screening for a modulator of activity or of latency or predispositio to an ORFX-associated disorder, said method comprising:
  - a) contacting a test compound with the polypeptide of claim 10; and
- b) determining if said test compound binds to said polypeptide, wherein binding of said test compound to said polypeptide indicates the test compound is a modulator of activity or of latency or predisposition to an ORFX-associated disorder.
- 21. A method for screening for a modulator of activity or of latency or predisposition to an ORFX-associated disorder, said method comprising:
  - a) administering a test compound to a test subject at an increased risk ORFX-associated disorder, wherein said test subject recombinantly expresses a polypeptide encoded by the nucleotide of claim 1:



- b) measuring expression the activity of said protein in said test subject;
- measuring the activity of said protein in a control subject that recombinantly expresses said protein and is not at increased risk for an ORFX-associated disorder; and
- d) comparing expression of said protein in said test subject and said control subject, wherein a change in the activity of said protein in said test subject relative to said control subject indicates the test compound is a modulator or of latency of predisposition to an ORFX-associated disorder.
- 22. The method of claim 20, wherein said test animal is a recombinant test animal that expresses a test protein transgene or expresses said transgene under the control of a promoter at an increased level relative to a wild-type test animal, and wherein said promoter is not the native gene promoter of said transgene.
- 23. A method for determining the presence of or predisposition to a disease associated with altered levels of a polypeptide of claim 11 in a subject, the method comprising:
  - a) measuring the amount of the polypeptide in a sample from said subject; and
  - b) comparing the amount of said polypeptide in step (a) to the amount of the polypeptide present in a control sample,

wherein an alteration in the level of the polypeptide in step (a) as compared to the control sample indicates the presence of or predisposition to a disease in said subject.

- 24. The method of claim 23, wherein said subject is a human.
- 25. A method for determining the presence of or predisposition to a disease associated with altered levels the nucleic acid molecule of claim 1 in a subject, the method comprising:
  - a) measuring the amount of the nucleic acid in a sample from the mammalian subject; and
  - b) comparing the amount of said nucleic acid in step (a) to the amount of the nucleic acid present in a control sample,

wherein an alteration in the level of the nucleic acid in step (a) as compared to the corsample indicates the presence of or predisposition to said disease in said subject.

- 26. The method of claim 25, wherein said subject is a human.
- 27. A method of treating or preventing a pathological condition associated with at ORFX-associated disorder in a subject, the method comprising administering to said subject polypeptide of claim 10 in an amount sufficient to alleviate or prevent said pathological condition.
  - 28. The method of claim 27, wherein said subject is a human.
- 29. A method of treating or preventing a pathological condition associated with at ORFX-associated disorder in a subject, the method comprising administering to said subject nucleic acid molecule of claim 1 in an amount sufficient to alleviate or prevent said pathological condition.
  - 30. The method of claim 29, wherein said subject is a human.
- 31. A method of treating or preventing a pathological condition associated with ar ORFX-associated disorder in a subject, the method comprising administering to said subject antibody of claim 12 in an amount sufficient to alleviate or prevent said pathological conditions.
  - 32. The method of claim 31, wherein said subject is a human.

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### (19) World Intellectual Property Organization International Bureau



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For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(75) Inventors/Applicants (for US only): SHIMKETS,

(54) Title: NUCLEIC ACIDS INCLUDING OPEN READING FRAMES ENCODING POLYPEPTIDES; "ORFX"

(57) Abstract: The present invention provides open reading frames encoding isolated polypeptides, as well as polynucleotides encoding ORFX and antibodies that immunospecifically bind to ORFX or any derivative, variant, mutant, or fragment of the ORFX polypeptides, polynucleotides or antibodies. The invention additionally provides methods in which the ORFX polypeptide, polynucleotide and antibody are used in detection and treatment of a broad range of pathological states, as well as to other uses.

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A. CLAS	SIFICATION OF SUBJECT MATTER			00,00021
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1	C12N15/11 C12N15/62	A01K67/027	A61K38/00	• •
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B. FIELD	DS SEARCHED			
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C. DOCUM	ENTS CONSIDERED TO BE RELEVANT			
Category °	Citation of document, with indication, where appropri	ate, of the relevant passa	oes	
				Relevant to claim No.
Α	COLE S.T.: "Deciphering t	the biology o	F	
	mycobacterium tuberculosis	from the	'	
	complete genome sequence." NATURE.	1		
	vol. 393, 11 June 1998 (19	98-06-11)		
	XP002144873	JO 00 11),		
	sequence			
A	LAMERDIN J.E.: "Sequence	analysis of =		
	3.5 MD contig in human 19p	13.3 containi	na	
	a serine protease gene clu	ster."		
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χ Furthe	er documents are listed in the continuation of box C.	Pate	ent family members are list	ed in annov
Special cate	gories of cited documents :			od II/ dililex.
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	NL - 2280 HV Hijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl.	1		
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Form PCT/ISA/210 (second sheet) (July 1992)



Interna | Application No PCT/US 00/08621

	tion) DOCUMENTS CONSIDERED TO BE RELEVANT						
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.					
P,X	M.D. ADAMS ET AL.: "The genome sequence of Drosophila melanogaster." SCIENCE, vol. 287, 24 March 2000 (2000-03-24), pages 2185-2195, XP002144875 the whole document	6					
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### **INTERNATIONAL SEARCH REPORT**



onal application No. PCT/US 00/08621

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)	
This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:	
Claims Nos.:     because they relate to subject matter not required to be searched by this Authority, namely:	
Although claims 27 to 32 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.	
Claims Nos.:  because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:	
3. Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).	
Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)	
This International Searching Authority found multiple inventions in this international application, as follows:	
see additional sheet	
As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.	
2. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.	
3. As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:	
A. No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:  Claims 1 to 32 partially	
Remark on Protest  The additional search fees were accompanied by the applicant's protest.  No protest accompanied the payment of additional search fees.	